

Reply
U.S.S.N. 09/ 757,202
Applicant Miller et al.
Page 3 / 11

Amendment to the Claims

Claims 1-14 and 31-59 were previously canceled. Claims 60-76 were previously added. Claim 15 is currently amended. A listing of all claims is presented below as they currently stand in this application following entry of this amendment.

Listing of claims:

1-14. Canceled

15. (currently amended) A method for making a water insoluble biocompatible composition, said method comprising combining, in an aqueous mixture, one or more polyanionic polysaccharides, a modifying compound, a nucleophile, and an activating agent under conditions sufficient to form said composition wherein said one or more polyanionic polysaccharides and said activating agent react to form a first activated species of said one or more polyanionic polysaccharides and wherein said modifying compound causes the formation of a new active carbonyl group on said second activated species polyanionic polysaccharide from said first activated species.

16. (original) The method of claim 15 wherein two or more polyanionic polysaccharides are employed.

17. (original) The method of claim 15 or 16 wherein said polyanionic polysaccharides are chosen from the group consisting of carboxymethyl cellulose, carboxymethyl amylose, hyaluronic acid, chondroitin-6-sulfate, dermatin sulfate, heparin, and heparin sulfate.

18. (original) The method of claim 15 wherein said polyanionic polysaccharide is hyaluronic acid.

19. (original) The method of claim 15 wherein said polyanionic polysaccharide is carboxymethyl cellulose.

20. (original) The method of claim 15 wherein said polyanionic polysaccharide is carboxymethyl amylose.

21. (original) The method of claim 16 wherein two polyanionic polysaccharides are hyaluronic acid and carboxymethyl cellulose.

22. (original) The method of claim 15 wherein said modifying compound is chosen from the group consisting of 1-hydroxybenzotriazole hydrate, 1-hydroxybenzotriazole monohydrate, N-hydroxysulfosuccinimide, N-hydroxysuccinimide, 4-nitrophenol, 2-nitrophenol, 4-nitrothiophenol, 2-nitrothiophenol, pentachlorophenol, pentafluorophenol, imidazole, tetrazole, and 4-dimethylaminopyridine.

Reply
U.S.S.N. 09/ 757,202
Applicant Miller et al.
Page 4 / 11

23. (original) The method of claim 15 wherein said activating agent comprises a carbodiimide.

24. (original) The method of claim 23 wherein said carbodiimide comprises 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide, or 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide methiodide.

25. (original) The method of claim 15 wherein said polyanionic polysaccharide is present in a concentration of 0.0002 - 0.1 M.

26. (original) The method of claim 25 wherein said polyanionic polysaccharide is present in a concentration of 0.0005 to 0.02M.

27. (original) The method of claim 15 wherein said method is carried out at a pH 3.5 -8.0.

28. (original) The method of claim 15 wherein the stoichiometry of said polyanionic polysaccharide to said activating agent is at least 0.1 molar equivalent of said activating agent per molar equivalent of said polyanionic polysaccharide.

29. (original) The method of claim 15 wherein the stoichiometry of said modifying agent to said activating agent is at least 1 molar equivalent of said modifying compound per molar equivalent of said activating agent.

30. (original) The method of claim 15 wherein said nucleophile is chosen from the group consisting of an amino acid amide, a monofunctional amine, an amino acid ester, an amino alcohol, an amino thiol, an amino phenol, an amino catechol, an amino acid, a salt of an amino acid, a peptide, and a protein.

31-59. Canceled.

60. (previously presented) A water insoluble composition prepared according to the method of claim 15 or 16.

61. (previously presented) The composition of claim 60 wherein said composition is in the form of a gel.

62. (previously presented) The composition of claim 60 wherein said composition is in the form of fibers.

63. (previously presented) The composition of claim 60 wherein said composition is in the form of a membrane.

Reply
U.S.S.N. 09/ 757,202
Applicant Miller et al.
Page 5 / 11

64. (previously presented) The composition of claim 60 wherein said composition is in the form of a foam.

65. (previously presented) The composition of claim 60, further comprising a drug dispersed within said composition.

66. (previously presented) The composition of claim 65 wherein said drug is chosen from the group consisting of proteins, biopolymers, and biologically compatible synthetic polymers.

67. (previously presented) The composition of claim 60 wherein said polyanionic polysaccharides are chosen from the group consisting of carboxymethylcellulose, carboxymethylamylose, hyaluronic acid, chondroitin-6-sulfate, dermatin sulfate, heparin and heparin sulfate.

68. (previously presented) The composition of claim 60 wherein said polyanionic polysaccharide is hyaluronic acid.

69. (previously presented) The composition of claim 60 wherein said polyanionic polysaccharide is carboxymethylcellulose.

70. (previously presented) The composition of claim 60 wherein said polyanionic polysaccharide is carboxymethylamylose.

71. (previously presented) The composition of claim 60 wherein two of said polyanionic polysaccharides are hyaluronic acid and carboxymethylcellulose.

72. (previously presented) The composition of claim 60 wherein said nucleophile is chosen from the group consisting of an amino acid amide, a mono functional amine, an amino acid ester, an amino alcohol, an amino thiol, an amino phenol, an amino catechol, an amino acid, a salt of an amino acid, a peptide, and a protein.

73. (previously presented) The composition of claim 60 further comprising a protein dispersed within said composition.

74. (previously presented) The composition of claim 60 wherein said modifying compound is chosen from the group consisting of 1 -hydroxybenzotriazole hydrate, 1 hydroxybenzotriazole monohydrate, *N*-hydroxysulfosuccinimide, *N*-hydroxysuccinimide, 4-nitrophenol, 2-nitrophenol, 4-nitrothiophenol, 2-nitrothiophenol, pentachlorophenol, pentafluorophenol, imidazole, tetrazole, and 4-dimethylaminopyridine.

75. (previously presented) The composition of claim 60 wherein said activating agent comprises a carbodiimide.

Reply
U.S.S.N. 09/ 757,202
Applicant Miller et al.
Page 6 / 11

76. (previously presented) The composition of claim 75 wherein said carbodiimide comprises 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, or 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide methiodide.